

MULTIPLE DISPLACEMENT AMPLIFICATION

Disclosed are compositions and a method for amplification of nucleic acid sequences of interest. The method is based on stand displacement replication of the nucleic acid sequences of interest by multiple primers. In one preferred form of the method, referred to as multiple strand displacement amplification, two sets of primers are used, a right set and a left set. The primers in the right set are complementary to one strand of the nucleic acid molecule to be amplified and the primers in the left set are complementary to the opposite strand. The 5' end of primers in both sets are distal to the nucleic acid sequence of interest when the primers have hybridized to the nucleic acid sequence molecule to be amplified. Amplification proceeds by replication initiated at each primer and continuing through the nucleic acid sequence of interest. A key feature of this method is the displacement of intervening primers during replication by the polymerase. In another preferred form of the method, referred to as whole genome strand displacement amplification, a random set of primers is used to randomly prime a sample of genomic nucleic acid (or another sample of nucleic acid of high complexity). By choosing a set of primers which are sufficiently random, the primers in the set will be collectively, and randomly, complementary to nucleic acid sequences distributed throughout nucleic acid in the sample. Amplification proceeds by replication with a highly processive polymerase initiated at each primer and continuing until spontaneous termination. A key feature of this method is the displacement of intervening primers during replication by the polymerase. In this way, multiple overlapping copies of the entire genome to be synthesized in a short time.

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